

### **REMARKS**

In the office action, claims 4, 5, and 7-13 have been objected to, and claims 1-3 and 6 have been rejected. Claims 14-18 have been withdrawn as directed to a non-elected invention. In response, Applicants have cancelled claims 1-18, added new claims 19-53, and provide the herein remarks. Claims 19-53 are pending in the application.

### **Support for New Claims**

Support for new claims 19-53 can be found in original claims 1-18 and in the specification beginning on the bottom of page 4 through page 6.

### **The Invention**

The present invention provides a method for preparing *in vitro* pancreatic cells capable of secreting insulin. The method utilizes exocrine cells which count for more than 95% of the cells present in pancreatic tissue, rather than using isolated stem cells.

Applicants have surprisingly discovered that inducing dedifferentiation of exocrine cells under the claimed culture conditions produces ductal precursor cells. The ductal precursor cells grown under the claimed culture conditions induce transformation of the cells into insulin secreting endocrine cells.

### **Claims Objections**

Claims 4, 5 and 7-13 have been objected to as being in improper form because a multiple dependent claim can not depend on other multiple dependent claims. In response, Applicants have cancelled claims 4, 5 and 7-13. Accordingly, the objection to the claims has been rendered moot.

### **Rejections Under 35 U.S.C. §112, Second Paragraph**

Claims 1-3 and 6 have been rejected under §112, second paragraph, as being indefinite for reciting the term “possibly,” and for allegedly not clearly claiming the positive steps of the method. In response, claims 1-3 and 6 have been cancelled. New claims 19-53

do not contain the term “possibly,” and clearly claim the positive steps of the method. Accordingly, the rejection of claims 1-3 and 6 has been rendered moot.

**Rejections Under 35 U.S.C. §103(a)**

Claims 1-3 and 6 have been rejected under §103(a) as being unpatentable over Bonner-Weir et al. (PNAS, July 5, 2000; vol. 97, no.14:7999-8004) or Bonner-Weir et al. (WO 00/78929).

According to the Examiner, both Bonner-Weir et al. documents teach the enzymatic isolation of pancreatic cells, the dedifferentiation thereof, and the subsequent dedifferentiation into insulin producing cells.

The Examiner notes that it is not clear if Bonner Weir et al. disclose all of the claimed limitations. However, according to the Examiner, the references clearly indicate that the various proportions and amounts of ingredients used in the claimed method are result effective variables that would be routinely optimized by the skilled practitioner.

The Examiner contends that because “the references clearly set forth which cells are to be isolated from the pancreas, using any known method to do so would have been obvious at the time the invention was made.” See page 4 of the office action. Applicants respectfully disagree.

The PNAS 97 document discloses a method for preparing pancreatic cells capable of secreting insulin from pancreatic duct cells. In the method, density gradients are used to separate the different pancreatic cells. Importantly, the preferred cells utilized are not recovered from the pellet of the gradient. PNAS 97 discloses that the pellet of the gradient contains less than 1% islet cells, and that these cells do not secrete insulin when grown in culture. See page 7999, right column, first full paragraph, and page 8002, left column, first paragraph.

The present invention utilizes exocrine cells obtained from the pellet formed as a result of density gradient centrifugation. As mentioned above, PNAS 97 teaches away from

using cells obtained from the pellet of the gradient when attempting to culture cells that will secrete insulin.

Accordingly, Applicants respectfully submit that the claimed invention is not unpatentable in view of PNAS 97.

The WO document discloses a method for preparing pancreatic cells capable of secreting insulin from pancreatic duct cells. In the WO document, the cells are separated after being cultured in a flask. The cells that do not attach to the flask are removed. The WO document does not disclose or suggest the separation of cells using density gradient centrifugation.


As discussed above, the present invention utilizes density gradient centrifugation to separate exocrine cells from the cell population. Therefore, because the WO document does not disclose or suggest all of the claim limitations, the present invention can not be unpatentable over the WO document.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-3 and 6 based on PNAS 97 and the WO document.

Applicants respectfully request that the Examiner consider claims 22 and 25 in particular as being patentable independently of the other claims.

It is now believed that this application is in condition for allowance. If resolution of any remaining issues is required prior to allowance of the application, and the Examiner believes a telephone discussion with Applicants representative may be helpful, she is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,



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